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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/073,065	02/12/2002	Shyam S. Mohapatra	USF-T156X	2390

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EXAMINER	
LUCAS, ZACHARIAH	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 11/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/073,065	MOHAPATRA ET AL.	
	Examiner	Art Unit	
	Zachariah Lucas	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 July 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *33-49* is/are pending in the application.

4a) Of the above claim(s) *37-49* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *33-36, 50-53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10-18-04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. Currently, claims 33-49 are pending in the application. In the prior action, mailed on April 5, 2004, claims 3, and 21-32 were under consideration and rejected. Claims drawn to methods had previously been restricted from the product claims in the Restriction Requirement of July 15, 2003. In the Response to the prior action, filed on July 8, 2004, the Applicant cancelled claims 3 and 21-32, and added new claims 33-49. Additionally, in a Supplemental Response filed on September 10, 2004, the Applicant added new claims 50-53.

2. New claims 37-49 are drawn to methods of making and using the claimed products. These claims are withdrawn from consideration as drawn to non-elected inventions.

3. Currently, claims 33-36 and 50-53 are under consideration.

Information Disclosure Statement

4. The information disclosure statement (IDS) submitted on October 18, 2004 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement has been considered by the examiner.

Specification

5. **(Prior Objection- Withdrawn)** The specification was objected to in the prior action as failing to provide proper antecedent basis for the claimed subject matter. See, 37 CFR 1.75(d)(1)

and MPEP § 608.01(o). In view of the cancellation from the claims of the subject matter lacking antecedent basis in the specification, the objection is withdrawn.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. **(Prior Rejection- Withdrawn)** Claims 3, and 21-32 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In view of the cancellation of the claims, the rejection is withdrawn.

8. **(Prior Rejection- Withdrawn)** Claims 21-23 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In view of the cancellation of these claims, the rejection is withdrawn.

9. **(Prior Rejection- Withdrawn)** Claims 29 and 31 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It was unclear if the phrase "wherein said composition comprises one or more plasmid DNA encoding an M2 RSV polypeptide and at least three RSV polypeptides selected from the group consisting of F, G, M, SH, NSI, NS2, N, and P" required that the composition comprise at least one DNA encoding the M2 polypeptide, and also is requiring at least three polypeptides from the indicated group, or if the claim is

requiring the presence of at least one DNA plasmid encoding the M2 polypeptide, and wherein said at least one DNA plasmid also encodes the at least three polypeptides selected from the group. In view of the Applicant statement (page 6 of the Response) that the composition comprises only plasmid DNAs (and chitosan), which plasmids encode the indicated antigens, the rejection is withdrawn.

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. **(Prior Rejection- Withdrawn)** Claims 23, 26-32 were rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. In view of the cancellation of the claims from the application, the rejection is withdrawn.

Claim Rejections - 35 USC § 102

12. **(Prior Rejection- Withdrawn)** Claims 3, and 24, and 25 were rejected under 35 U.S.C. 102(b) as being anticipated by Murphy et al., U.S. Patent 5,882,651. In view of the cancellation of the claims, the rejection is withdrawn.

Claim Rejections - 35 USC § 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. **(Prior Rejection- Withdrawn)** In the prior action, claims 3, and 21-24 were rejected under 35 U.S.C. 103(a) as obvious over the teachings of Collins (U.S. Patent 6,264,957) in view of Connors (J. Virol 65(3): 1634-37). Claims 3 and 21-24 have been cancelled and claims 33-36 inserted in their stead. The new claims require that the claimed plasmids be in coacervate with chitosan. In view of this amendment, and because neither of Collins not Connors teaches the use of chitosan for the delivery of plasmid DNA, the rejection is withdrawn.

15. **(Prior Rejection-Withdrawn)** Claims 3 and 24 were rejected under 35 U.S.C. 103(a) as being unpatentable over Conners et al., supra. The claims of the application have been amended as indicated above. For the reasons indicated above, the rejection is withdrawn.

16. **(Prior Rejection-Withdrawn)** Claims 21-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Conners in view of Cates et al., WO98/02457. The claims of the application have been amended as indicated above. For the reasons indicated above, the rejection is withdrawn.

17. **(Prior Rejection-Withdrawn)** Claim 25 is rejected under 35 U.S.C. 103(a) as being unpatentable over Conners as applied to claims 3 and 24 above, and further in view of Domachowske et al., Clin Microbiol Rev 12(2): 298-309. The claims of the application have been amended as indicated above. For the reasons indicated above, the rejection is withdrawn.

18. **(Prior Rejection-Withdrawn)** Claims 3 and 24-27, 29, 30, and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Conners as applied to claim 3 above, and further in view of the teachings of Li et al. (J Exp Med 188(4): 681-88) and Li et al. (Virology, 269: 54-65) and in light of the teachings of Montgomery et al., Phamacol Ther 74(2): 195-205). The claims

of the application have been amended as indicated above. For the reasons indicated above, the rejection is withdrawn.

19. **(Prior Rejection- Withdrawn)** Claims 28 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Conners (J. Virol 65(3): 1634-37) in view of the teachings of the Li references (J Exp Med 188(4): 681-88, and Virology, 269: 54-65), and further in view of Leong et al., J Controlled Release 53: 183-93. These claims have been cancelled from the application; the rejection is therefore withdrawn.

20. **(New Rejection- Necessitated by Amendment)** Claims 33, 34, and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Connors (J. Virol 65(3): 1634-37) in view of the Li references (J Exp Med 188(4): 681-88, and Virology, 269: 54-65), and further in view of Leong (J Controlled Release 53: 183-93) as applied against claims 28 and 31 in the prior action. Claim 34 is treated as representative of the rejected claims. This claim reads on an immunogenic composition comprising one or more plasmid DNA molecules coacervated with chitosan, wherein the plasmids encode each of the M2, F, and G antigens of RSV, and also encode at least one additional antigen selected from the group consisting of the M, SH, NS1, NS2, N, and P RSV proteins. Claim 36 further limits the invention to embodiments wherein the plasmid DNA/chitosan coacervates form into nanospheres.

The teachings of these references, as well as the supportive teachings of Montgomery et al (Pharmacol Ther 74:195-205) have been described in the prior action. In the prior action, the claims read on a combination of protein antigens and plasmid DNAs. The claims have now been amended to read on compositions requiring the presence of only the plasmid DNAs. However, in

view of the teachings of the Li and Leong references, the currently claimed composition would still have been obvious to those in the art. This is for substantially the same reasons and indicated in the rejections of parts 24 and 25 of the prior action. Thus, while the rejection is withdrawn as to claims 28 and 31 as described above, the rejection is extended to new claims 33, 34, and 36.

It is noted that the Applicant has provided grounds for traversal of the rejection of now cancelled claims 28 and 31 which may also apply against the rejection of claims 33, 34, and 36. The arguments in traversal consist of a recitation of the differences between each of the separate cited references and the claimed invention, and statements that no one of the cited references provides motivation or suggestion to make the claimed invention. However, "one cannot show non-obviousness by attacking references individually where, as here, the rejections are based on combinations of references." In re Young, 159 U.S.P.Q. 725, at 728 (CCPA, 1968); and In re Keller, Terry, and Davies, 208 USPQ 871, at 882 (CCPA, 1981). Thus, because the Applicant's arguments in traverse are based on the differences between each of the different references individually, and not what is taught collectively as laid out in the prior action, the traversal is not found persuasive.

The Applicant additionally argues that the only teachings suggesting that the claimed composition (coacervates of plasmid DNA encoding RSV antigens and chitosan) would be effective in inducing an immune response (and achieving other benefits as opposed to other compositions) are found in the Applicant's own disclosure. However, this argument is also not found persuasive. This is because of the inclusion of the teachings in the Li references and Leong. The Li references indicate that DNA vaccines are effective in inducing immune responses against RSV antigen. In particular, the reference in the Virology (269: 54-65) article

indicates that plasmid DNA compositions are able to induce immune responses against encoded antigens. Further, the article also teaches that the DNA plasmids were able to induce such responses with a lack of the enhanced lung disease seen with other vaccines. Page 61. Further, the Leong reference teaches that chitosan/DNA nanospheres are effective delivery vehicles of plasmid DNA, and that such vehicles have low toxicity. See e.g., page 91. Thus, these teachings, in addition to the teachings indicated in the prior action, provide both motivation and reasonable expectation of success in the use of plasmid DNA/chitosan vehicles for the delivery of DNA compositions encoding RSV antigens for the induction of an anti-RSV immune response. The Applicant's argument that the rejection is merely an obvious to try rejection is therefore not found persuasive.

21. **(New Rejection- Necessitated by Amendment)** Claim 35 is rejected under 35 U.S.C. 103(a) as being unpatentable over Connors in view of the Li references, and further in view of Leong as applied in part above. Claim 35 requires that the indicated DNA plasmids encode each of the M2, F, G, M, SH, NSI, NS2, N, and P RSV antigens.

The teachings of Connors have been described in part in the prior action. The reference teaches that each of the indicated proteins* was capable of inducing an immune response against RSV. See, page 1635. Thus, it would have been obvious to those in the art to use a composition comprising each of these antigens to induce an anti-RSV immune response. These teachings, in combination with the teachings of the Li and Leong references as described above and in the

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* It is noted that the Connors reference teaches the antigen 1B and 1C instead of NS1 and NS2. However, as can be seen in the teachings of Pastey et al., J Gen Virol 76: 193-97, the 1B and 1C antigens are, respectively, the same as the NS2 and NS1 antigens.

prior action, render obvious such compositions comprising coacervates of plasmid DNAs encoding these antigens and chitosan. These references therefore render obvious the composition of claim 35.

This rejection is considered a new rejection necessitated by amendment. While it is noted that certain claims in the application at the time the prior action was mailed referred to chitosan/plasmid DNA compositions, none of these claims were drawn to the specific compositions now claimed. In particular, neither of claims 28 nor 31 required any particular set of antigens to be encoded by the DNA plasmids coacervated with chitosan. Claim 23 of the prior action further limits claim 21. Claim 21 described embodiments wherein the protein M2 antigen and at least three other RSV antigens are antigens encoded by plasmid DNAs. Claim 23 limits the claims to embodiments wherein the plasmid DNAs were coacervated with chitosan. However, the limitations of claims 21 and 23 were not given patentable weight in the claims as they merely defined the source of the claimed antigens. The claims were drawn to compositions comprising plasmid DNAs encoding the M2 and other antigens coacervated with chitosan, but to the antigens themselves.

Because the previously pending claims were not drawn to the currently claimed compositions, the new rejection over the new claims drawn to previously unclaimed embodiments, is necessitated by amendment.

22. **(New Rejection- Necessitated by Amendment)** Claims 50-53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Connors in view of the Li references and Leong as applied against claims 33-36 above, and further in view of Illum (WO 90/09780) and Rolland et

al. (U.S. 6,184,037). These claims are substantially identical to claims 33-36, except that they limit the immunogenic compositions to embodiments wherein the composition is an inhalant. The teaching of Connors, the Li references, and Leong have been described above and in the prior actions. While these references suggest immunogenic compositions comprising RSV antigen-encoding plasmids encapsulated by chitosan nanospheres, the references do not explicitly suggest the formulation of such compositions as inhalants.

However, the Connors reference teaches that administration of a recombinant virus that expresses RSV proteins induced protective immune responses in mice. Page 1635. See also, Wyatt et al., Vaccine 18: 392-97 (of record in the May 2002 IDS- teaching on pages 394 and 395 the use of similar vectors intranasally administered as an immunogenic composition). In addition, each of the Illum and Rolland references teach that chitosan microparticles encapsulating DNA may be administered as an inhalant. Illum, pages 7 and 8 (teaching that chitosan particles comprising RSV vaccines may be nasally administered- including through aerosolization); and Rolland, column 11 lines 38-44 (teaching that chitosan encapsulating particles may be administered as inhalants, including by aerosolization of the particles). Thus, these three references teach the administration of anti-RSV vaccines as intranasally, teach that such intranasal administration may be achieved through formulation as an inhalant, and indicate that chitosan microparticles would be an effective means of delivery of the plasmids as an inhalant.

In combination with the teachings of the Li references and Leong as applied to claim 33-36, the cumulative teachings of these references both suggest the claimed inventions, and

provide a reasonable expectation of success in the use of the compositions to induce an immune response against RSV.

Conclusion

23. No claims are allowed.

24. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

25. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 571-272-0905. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Z. Lucas
Patent Examiner

James C. Housel 11/15/04

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